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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,928	MERCKEN ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed 6/2/08 is acknowledged. Claims 1, 12 and 13 are cancelled. Claims 2-6, 8, 9, 11, and 14-16 are amended. Claims 2-11 and 14-16 are pending in this application and under examination in this office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

3. Applicant's arguments filed on 6/2/08 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Objections

4. Claims 14 and 16 are objected to because of the following informalities: "HCHWA-D" is not a common abbreviation in the art. Applicants are required to spell out "HCHWA-D" at the first usage. Appropriate correction is required.

Claim Rejections/Objections Withdrawn

5. The rejection of Claims 3, 5, 6, 8, 14 and 15 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendment to the claims.

Claim Rejections/Objections Maintained

In view of the amendment filed on 6/2/08, the following rejections are maintained.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-5, 8, 9, 11 and 14-16 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383), Pirttila et al. (J. Neurol Sci. 1994 Dec 1; 127:90-5), WO0162801 (as in IDS submitted on Mar 23, 2005) or Naslund et al (as in IDS submitted on Mar 23, 2005). The rejection is maintained for the reasons made of record.

On p. 6-8 of the response, Applicant argues that Walker et al., Pirtila, WO0162801 and Naslund do not dislcose antibodies that bind to Aβ11-x without cross-reacting with the full length of Aβ1-40/42 as presently claimed. Applicant argues that the epitopes of Aβ11-15 and Aβ11-17 are not necessarily encompassed within the epitopes of 10D5 (Aβ1-16), 6E10 (Aβ1-16), 4G8 (Aβ17-24) and 266 (Aβ13-28). Applicant further cites Immunology by I. Roitt, J. Brostoff, D. Male in support of the arguments. Applicant's arguments have been fully considered but they are not persuasive.

In response, as previously made of record, the art antibodies raised against Aβ1-16 (10D5 & 6E10, Walker and Naslund), Aβ17-24 (4G8, Prittila), and Aβ13-28 (266, WO01/62801) immungens can bind to the epitopes of Aβ11-x as evidenced by Huse et

al (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284, cited in the previuos office action). With regard to whether the art antibodies have the same property as the claimed antibodies that bind to Aβ11-x without cross reacting with the full length of Aβ1-40/42, it is noted that Applicant claims a product in terms of a function, property or characteristics is the same as the prior art products. Note that

"Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See MPEP § 2112.01 [R-3].

As previuosly made of record, if the epitope to which Applicant's antibody binds is present in Aβ11-x, so that Applicant's antibody binds to Aβ11-x, it is also present in Aβ 1-16, 17-24, and 13-28. Applicant fails to provide side-by-side comparisons to demonstrate that the claimed antibody is different from those antibodies disclosed by Walker et al., Pirtila, WO0162801 and Naslund. It is also known in the art that anti-Aβ antibodies can cross react with different species or different lengths of Aβ peptides in different titrations because of their different binding affinity. Applicant has provided no showing that the antibodies in the art have characteristics different from those specifed by Applicant and do not in fact cross react with the full length of Aβ1-40/42 in the same titration or at the same concentration as those of the prior art. Since the claimed antibody is substantially identical in structure or composition and is able to bind to Aβ11-x, the antibodies disclosed by Walker et al., Pirtila, WO0162801 and Naslund farily anticipate the claimed antibody because Applicant fails to demonstrate that the claimed

antibody has a function, property or characteristics different from the antibodies dislcosed by the art. Accordingly, the rejection of claims 2-5, 8, 9, 11 and 14-16 under 35 U.S.C. 102 (b) as being anticipated by Walker et al., Pirttila et al., WO0162801 or Naslund et al. is maintained.

7. Claims 2, 5, 8, and 14-16 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Solomon et al. (Proc. Natl. Acad. Sci. USA. 1996. 93: 452-455). Claims 2, 5, 8, and 14-16 stand rejected under 35 U.S.C. 102 (a) as being anticipated by Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284). The rejections are maintained for reasons made of record.

On p. 8 of the response, Applicant argues that the reference of Solomon et al. does not teach the claimed antibody because Solomon teaches antibodies AMY-33 and 6F/3D, which are specific to Aβ1-28 and Aβ8-17. Applicant also argues that Huse does not teach the claimed antibody because Huse teaches antibodies BAN50, BNT77 and 4G8, which are specific to Aβ1-10, Aβ11-16 and Aβ1-40/11-30/1-34/11-34 respectively. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the antibodies raised against Aβ 1-28 and 8-17 taught by Solomon et al. would inherently recognize Aβ11-x because the amino acid sequence of the immunogens (5-7 amino acids of Aβ11-x) for the instant antibodies are encompassed within the sequences of amino acids 1-28 and 8-17 of Aβ. For the same reason, the antibody BNT77 taught by Huse et al. was raised against amino acids 11-16 of Aβ, thus it can recognize N-terminal truncated species of Aβ.

It is known in the art that anti-Abeta antibodies can cross react with different species or length of Aβ peptides in different titrations. Applicant has provided no showing that the antibodies in the art have characteristics different from those specifed by Applicant and do not in fact cross react with the full length of Aβ1-40/42 in the same titration. In addition, if the epitope to which Applicant's antibody binds is present in Aβ11-x, so that Applicant's antibody binds to Aβ11-x, it is also present in Aβ 11-16, 1-28 and 8-17. Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2-5, 8, 9, 11 and 14-16 stand rejected under 35 U.S.C. 103(a) for being unpatentable over Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284) in

view of Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383) and WO0162801. The rejection is maintained for the reasons made of record.

On p. 8 of the response, Applicant argues that Huse et al., Walker and WO0162801 do not teach the claimed antibody because the combined references do not disclose or suggest the claimed antibodies specific for Aβ11-x peptides. Applicant's arguments have been fully considered but they are not persuasive.

In response, for the reasons set forth above at paragraphs 6-7, the antibodies disclosed by Huse et al., Walker et al. and WO0162801 do recognize Aβ11-x because the antibodies disclosed Huse et al., Walker et al. and WO0162801 have been shown to have the same property as the claimed antibodies. In addition, WO0162801 also teaches a method of detection of Aβ in the brain tissue and CSF of Alzheimer's disease patients using labeled antibodies by electrophoresis or ELISA as recited in claims 9-11 and 14 (see p.26, examples 1-2; p. 30, example 6). Thus, It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use the antibody raised against Aβ11-16 or use the antibody that can recognize Aβ11-x to detect Aβ11-x in Alzheimer's disease because the level of Aβ11-40/42 has been shown increased in AD patients. The person of ordinary skill in the art would have been motivated and have expected success in using an antibody that recognize Aβ11-x to detect diseases associated Aβ formation because the antibody against Aβ11-16 is able to detect Aβ11-40/42 in AD brains.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detection of Aβ11-40 in the CSF and brain section of Alzheimer's disease by using antibodies raised against Aβ peptides consisting of 6-8 amino acids of Aβ_11 (6AA) or Aβ_(8AA) (SEQ ID NOs: 1-4), does not reasonably provide enablement for using the antibodies that specifically bind to Aβ11-x peptides to diagnose all amyloid-related diseases as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The rejection is reinstated and maintained for the reasons made of record.

On p. 10 of the response, Applicant argues that the rejection is obviated by amendment to the claims. Applicant's argument has been fully considered but it is not persuasive.

In contrast, the specification only teaches diagnosis of AD with the claimed antibody but fails to teach diagnosis of other diseases as recited in instant claims 14 and 16. As previously made of record, the specification fails to provide sufficient guidance as to whether Down's syndrome, HCHWA-D or cerebral amyloid angiopathy can be diagnosed by the claimed method with the claimed antibody. The specification fails to provide guidance as to whether Aβ11-40 or other Aβ11-x can be found in these

diseases and how much levels of the Aβ11-x expression would be considered as an indicator of the disease. Therefore, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, undue experimentation would be required by a skilled artisan to practice the claimed invention.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On p.10 of the response, Applicant argues that the rejection is obviated by amendment to the claims. Applicant's argument has been fully considered but it is not persuasive.

In contrast, claim 16 still recites "support". As previously made of record, the specification fails to define/describe what is encompassed in the definition of "support". The disclosure fails to set forth the metes and bounds of what is encompassed within the definition of such support; thus the claim is indefinite.

Claim Rejections - 35 USC § 102/103

11. Claims 2, 6, 7, 15 and 16 stand rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 6984720 (Korman et al. issued on Jan 10, 2006, priority Aug 24, 1999). The rejection is maintained for the reasons made of record.

On p. 10 of the response, Applicant argues that Although the '720 patent discloses an antibody produced from a hybridoma cell line that is also named "5C4", the antibody of the '720 patent is raised against CTLA-4 not Ab11-x peptide as hybridoma cells J&JPRD/hAβ11/1 and -/2. Applicant's arguments have been fully considered but they are not persuasive.

As previously made of record, the 5C4 monoclonal antibody as disclosed by the '720 patent has the same name as described in the instant specification and also can block amyloid accumulation in Alzheimer's patients (see col.9, lines 47-62.). Applicant fails to demonstrate that the 5C4 monoclonal antibody disclosed by the '720 patent is structurally and functionally different from the claimed antibody (i.e. also named 5C4 as described on p.22 of the instant specification). Applicant fails to provide side-by-side comparisons to demonstrate that the claimed antibody is structurally and functionally different from the antibodies disclosed by the '720 patent. Since the 5C4 monoclonal antibody of the '720 patent can block amyloid accumulation in AD patients, it indicates that the 5C4 monoclonal antibody of the '720 patent has the same property and function as the claimed antibody, which is capable of binding to Aβ11-x, and thus the binding of

the '720 patent's 5C4 monoclonal antibody to Aβ11-x would be an inherent feature of the antibody. Note that

"Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. 'There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102.' In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA1977)." See MPEP § 2112 [R-3]

In addition,

"Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See MPEP § 2112.01 [R-3].

Claim Rejections - 35 USC § 103

12. Claims 2-11 and 14-16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284) in view of Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383 as cited in the previous office action) and WO0162801 (as in IDS submitted on Mar 23, 2005 and cited in the previous office action) as applied to claims 2-5, 8, 9, 11 and 14-16 above, and further in view of US Patent No. 6984720 (Korman et al. issued on Jan 10, 2006, priority Aug 24, 1999). The rejection is maintained for the reasons made of record.

On p. 11 of the response, Applicant argues that Huse et al., Walker et al., and WO0162801 do not teach antibodies that specifically recognize Aβ11-15/17 with binding specificity to Ab11-x peptides but not to full length Aβ1-40/42 and the '720 patent does

not teach hybridoma cell lines J&JPRD/hAβ11/1 and J&JPARD/hAβ11/2. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, Huse et al., Walker et al., and WO0162801 do teach antibodies recognizing Aβ11-15/17 with binding specificity to Aβ11-x as set forth above at paragraphs 6-8. In addition, the '720 patent teaches a monoclonal antibody named 5C4 that is capable of blocking amyloid accumulation in AD patients, which has the same name of J&JPRD/hAβ11/1 and J&JPARD/hAβ11/2 as described in the instant specification. Thus, it is obvious to a skilled artisan at the time the instant invention was made to generate an antibody raised against Aβ11-15 or 11-17 (SEQ ID NO:1-4) to substitute the antibodies of Huse et al., Walker et al., and WO0162801 by a hybridoma 5C4 (J&JPARD/hAβ11/2) as in instant claims 6-7 because the antibody of the hybridoma 5C4 can reduce amyloid accumulation, and antibodies against Aβ 1-16, 11-16, 1-28 and 8-17 can bind Aβ11-x. It is also obvious to substitute the antibodies of Huse et al., Walker et al., and WO0162801 by a hybridoma cell line named 5C4 (J&JPARD/hAβ11/2) in the methods of detecting or diagnosing AD to detect Aβ11-x in AD as recited in instant claim 10 because the antibody of the hybridoma 5C4 can reduce amyloid accumulation and the level of Aβ11-40/42 has been shown increased in AD patients.

Conclusion

13. NO CLAIM IS ALLOWED.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
September 8, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647